(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
17 May 2001 (17.05.2001)

PCT

(10) International Publication Number
WO 01/34809 A2

(51) International Patent Classification[7]: C12N 15/31, C07K 14/31, 16/12, C12Q 1/68, G01N 33/53, A61K 39/085, 48/00

(21) International Application Number: PCT/US00/30782

(22) International Filing Date:
9 November 2000 (09.11.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/164,258 9 November 1999 (09.11.1999) US

(71) Applicant *(for all designated States except US)*: **GLAXO GROUP LIMITED** [GB/GB]; Glaxo Wellcome House, Berkeley Avenue, Greenford, Middlesex UB6 0NN (GB).

(72) Inventor; and

(75) Inventor/Applicant *(for US only)*: **KIMMERLY, William, John** [US/US]; 242 Via Villena, Encinitas, CA 92024 (US).

(74) Agents: **LEVY, David, J.**; Glaxo Wellcome Inc., Five Moore Drive, P.O. Box 13398, Research Triangle Park, NC 27709-3398 et al. (US).

(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:
— *Without international search report and to be republished upon receipt of that report.*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 01/34809 A2

(54) Title: STAPHYLOCOCCUS EPIDERMIDIS NUCLEIC ACIDS AND PROTEINS

(57) Abstract: S epidermidis polypeptides and DNA (RNA) encoding such polypeptides and a procedure for producing such polypeptides by recombinant techniques is disclosed. Also disclosed are methods for utilizing such polypeptides and DNA (RNA) for the treatment of infection, particularly infections arising from S epidermidis. Antagonists against the function of such polypeptides and their use as therapeutics to treat infection are also disclosed. Also disclosed are diagnostic assays for detecting diseases related to the presence of S epidermidis nucleic acid sequences and the polypeptides in a host. Also disclosed are diagnostic assays for detecting polynucleotides and polypeptides related to S epidermidis.

STAPHYLOCOCCUS EPIDERMIDIS NUCLEIC ACIDS AND PROTEINS

Field of the Invention

The present invention provides nucleic acids, and peptides, polypeptides and proteins encoded by the nucleic acids, isolated from Staphylococcus epidermidis.

Background of the Invention

Staphylococcus epidermidis is a gram-positive bacteria present in the normal flora of humans, and is typically present on the skin. It is catalase positive and grows aerobically. It is inplicated in various human conditions and diseases, including subacute bacterial endocarditis (Baddour LM et al., Production of experimental endocarditis by coagulase-negative staphylococci: variability in species virulence, J. Infect. Dis. 150: 721-727, 1984; Karchmer AW, Archer GL, Dismukes WE, Staphylococcus epidermidis causing prosthetic valve endocarditis: microbiologic and clinical observations as guides to therapy, Ann Intern Med. 1983;98:447-455.) and septicemia (Christensen GD et al., Nosocomial septicemia due to multiply antibiotic-resistant Staphylococcus epidermidis, Ann. Intern. Med. 96: 1-10, 1982). S. epidermidis is estimated to be responsible for about 12% of all hospital patient infections. Because of the organism's peculiar ability to colonize polymer and metallic surfaces, there is a correlation of infection with the insertion of intravenous lines or catheters or implantation of prosthetic devices. Treatment can be difficult since different isolates of S. epidermidis show a broad spectrum of antibiotic resistance. The organism also produces a polysaccharide biofilm which helps to protect the bacteria from the human immune system (Tojo M et al., Isolation and characterization of a capsular polysaccharide adhesin from Staphylococcus epidermidis, J. Infect. Dis. 157: 713-722, 1988).

The present invention advantageously provides isolated nucleic acids and their encoded peptides, polypeptides and proteins from the genome of S. epidermidis, as well as the genomic map of S. epidermidis. Thus, the present invention fulfils a a widely-felt need for S.epidermidis diagnostics, antigens, and

About 26 different isolates of S. epidermidis have been submitted to ATCC listed in their on-line catalog, listed below:

1: ATCC Number: 146 Organism: Staphylococcus epidermidis
2: ATCC Number: 33501 Organism: Staphylococcus epidermidis
3: ATCC Number: 49741 Organism: Staphylococcus epidermidis
4: ATCC Number: 51625 Organism: Staphylococcus epidermidis
5: ATCC Number: 29997 Organism: Staphylococcus epidermidis
6: ATCC Number: 19654 Organism: Staphylococcus epidermidis
7: ATCC Number: 14389 Organism: Staphylococcus sp. deposit
8: ATCC Number: 14852 Organism: Staphylococcus epidermidis
9: ATCC Number: 49134 Organism: Staphylococcus epidermidis
10: ATCC Number: 13518 Organism: Staphylococcus epidermidis
11: ATCC Number: 9491 Organism: Staphylococcus epidermidis
12: ATCC Number: 35547 Organism: Staphylococcus epidermidis
13: ATCC Number: 35984 Organism: Staphylococcus epidermidis
14: ATCC Number: 35983 Organism: Staphylococcus epidermidis
15: ATCC Number: 700296 Organism: Staphylococcus epidermidis
16: ATCC Number: 49461 Organism: Staphylococcus epidermidis
17: ATCC Number: 29641 Organism: Staphylococcus epidermidis
18: ATCC Number: 29887 Organism: Staphylococcus epidermidis
19: ATCC Number: 29886 Organism: Staphylococcus epidermidis
20: ATCC Number: 55133 Organism: Staphylococcus epidermidis
21: ATCC Number: 27626 Organism: Staphylococcus sp. deposit
22: ATCC Number: 31874 Organism: Staphylococcus epidermid
23: ATCC Number: 14990 Organism: Staphylococcus epidermid
24: ATCC Number: 155 Organism: Staphylococcus sp. deposit
25: ATCC Number: 155-U Organism: Staphylococcus sp. depos
26: ATCC Number: 12228 Organism: Staphylococcus epidermid

Throughout this application, various publications are referenced. These publications are hereby incorporated by reference in their entirety.

While the invention has been described with respect to certain specific embodiments, it will be appreciated that many modifications and changes may be made by those skilled in the art without departing from the spirit of the invention. It is intended, therefore, by the appended claims, to cover all such modification and changes as fall within the true spirit and scope of the invention.

What is claimed is:

1. An isolated polynucleotide comprising a member selected from the group consisting of:

(a) a polynucleotide encoding a polypeptide having at least a 70% identity to a polypeptide set forth in the Sequence Listing;

(b) a polynucleotide which is complementary to the polynucleotide of (a); and

(c) a polynucleotide comprising at least 15 sequential bases of the polynucleotide of (a) or (b).

2. The polynucleotide of Claim 1 wherein the polypeptide has at least 80% identity to the polypeptide set forth in the Sequence Listing.

3. The polypeptide of Claim 2 wherein the polypeptide has at least 90% identity to the polypeptide set forth in the Sequence Listing.

4. The polynucleotide of Claim 1 wherein the polynucleotide is DNA.

5. The polynucleotide of Claim 1 wherein the polynucleotide is RNA.

6. The polynucleotide of Claim 4 wherein the polynucleotide has at least 80% identity to a polynucleotide set forth in the Sequence Listing.

7. The polynucleotide of Claim 6 wherein the polynucleotide has at least 90% identity to a polynucleotide set forth in the Sequence Listing.

8. The polynucleotide of Claim 4 comprising a polynucleotide set forth in the Sequence Listing.

9. The polynucleotide of Claim 4 comprising a polynucleotide set forth in the Sequence Listing as any of an odd-numbered SEQ ID Nos1-3334.

10. An isolated polynucleotide comprising a member selected from the group consisting of:

(a) a polynucleotide having at least a 70% identity to a polynucleotide contained in any of ATCC Deposit Nos. 146; 33501; 49741; 51625; 29997; 19654 ; 14389 ; 14852 ; 9134 ; 13518; 9491; 35547 ; 35984; 35983; 700296; 49461; 29641; 29887 ; 29886; 55133; 27626; 31874; 14990; 155; 155-U; 12228 and substantially encoding the polypeptide comprising amino acids 1 to 416 of SEQ ID NO:2;

(b) a polynucleotide complementary to the polynucleotide of (a); and

(c) a polynucleotide comprising at least 15 sequential bases of the polynucleotide of (a) or (b).

11. A vector comprising the DNA of Claim 4.

12. A host cell comprising the vector of Claim 11.

13. A process for producing a S. epidermidis polypeptide comprising expressing from the host cell of Claim 12 a polypeptide encoded by said DNA.

14. A process for producing a cell which expresses a S. epidermidis polypeptide comprising transforming or transfecting the cell with the vector of Claim 11 such that the cell expresses the polypeptide encoded by the DNA contained in the vector.

15. A polypeptide comprising an amino acid sequence which is at least 70% identical to a polypeptide set forth in the Sequence Listing.

16. A polypeptide comprising an amino acid sequence which is at least 80% identical to a polypeptide set forth in the Sequence Listing.

17. A polypeptide comprising an amino acid sequence which is at least 90% identical to a polypeptide set forth in the Sequence Listing.

18. A polypeptide comprising an amino acid sequence as set forth in the Sequence Listing.

19. An antibody against the polypeptide of claim 18.

20. An antagonist which reduces or inhibits the activity of the polypeptide of claim 18.

21. A method for the treatment of an individual having need to reduce or inhibit the activity of the polypeptide of Claim 18 comprising administering to the individual a therapeutically effective amount of the antagonist of Claim 20.

22. A complex of a polypeptide and a binding molecule which comprises the polypeptide of Claim 18 and a binding molecule that is capable of antagonising the activity of the polypeptide.

23. A process for diagnosing in a subject a disease related to expression of the polypeptide of claim 18 comprising detecting the presence in the subject of a nucleic acid sequence encoding said polypeptide.

24. A diagnostic process comprising detecting the presence of the polypeptide of claim 18 in a sample derived from a subject.

25. A method for identifying compounds capable of inhibiting the activity of the polypeptide of claim 18 comprising:

(a) contacting a cell expressing the polypeptide on the surface thereof with a selected compound, under conditions to permit binding to the polypeptide in the presence of a component capable of providing a detectable signal in response to the binding of the compound to said polypeptide; and

(b) detecting the presence or absence of a signal generated in response to the binding of the compound to the polypeptide,

the presence of a signal indicating a compound capable of inhibiting the activity of the polypeptide.

26. A method for inducing an immunological response in a mammal which comprises inoculating the mammal with the polypeptide of Claim 15, or a fragment or variant thereof, adequate to protect said animal against infection from S. epidermidis.

27. A method of inducing an immunological response in a mammal which comprises delivering a gene encoding the polypeptide of Claim 15, or a fragment or variant thereof, and obtaining expression of the gene *in vivo* in order to induce an immunological response to produce antibody to protect said animal against infection from S. epidermidis.

28. An immunological composition comprising a DNA capable of expressing a polypeptide of Claim 15 which, when introduced into a mammal, induces an immunological response in the mammal, and a pharmaceutically acceptable carrier.

29. An immunological composition comprising a polypeptide of claim 15 which, when introduced into a mammal, induces an immunological response in the mammal, and a pharmaceutically acceptable carrier.

rfA, MnhA, MnhB, MnhC, MnhD, MnhE, MnhF and MnhG, complete c
ds. NID: g4001723.
atgtttatgttgattggtattattggctcatttacaacaggagatattttcaacttgttt
gtgttctttgaagtctttttaatgtcttcatattgtttactcgttattggtactactaaa
atacaattacaagaaacaattaagtatattttagtcaatgttgtttcatcgtctttcttt
gtcatgggtgttgcagttttatattcagttgtaggaactttaaatctcgctcatattagt
gaaagattgtcacaactttctgtacatgacagtggcttagtcaatattgtttttatttta
tttatctttgtctttgccactaaagcaggcgtttttcctatgtacgtatggctacctggt
gcttattatgcccctccagtagcgatcatcacgttctttggtgcactattgactaaagtg
ggtgtatacgcaattgcgagaactctaagtttattctttaataatacagtaagcttttct
cattatgtcatccttttcttagcattacttacaattatttttggatgtataggtgcgata
gcttactatgatacgaagaaaatcatcctttacaatattatgattgcagtaggtgtcata
ttagttggtattgctatgatgaacgaatcaggcatgactggtgcaatatattacacacta
catgatatgttagttaaagcttcattgttcttactcattggcgtcatgtacaaaatcact
aaaacgactgacttacgtcattttggtggcttgataaaagggtatcctattctaggttgg
acatttctttattgcagcgctaagcttagcgggtataccacctttttagtggtttctacggt
aaatttctatattgttcgagcgacctttgaaaaaggattttatctaagtggtatcatgta
cttttatcaagtttaatcgtgttatattcagtcatacgtatttttcttaaaaggatttttc
ggtgaagttgaaggatatactttatctaaaaaggtaaatgttaaatatctaacaactatc
gctgttgcatctacagttattactgtaatctttggattatctgcagacacgttattccca
atcatcaaagatggcgctgaaacgtttgtcgatccaagtcaatatattcatagtgtgtta
ggaggtaaatag

Sequence 2026
MFMLIGIIGSFTTGDIFNLFVFFEVFLMSSYCLLVIGTTKIQLQETIKYILVNVVSSSFF
VMGVAVLYSVVGTLNLAHISERLSQLSVHDSGLVNIVFILFIFVFATKAGVFPMYVWLPG
AYYAPPVAIITFFGALLTKVGVYAIARTLSLFFNNTVSFSHYVILFLALLTIIFGCIGAI
AYYDTKKIILYNIMIAVGVILVGIAMMNESGMTGAIYYTLHDMLVKASLFLLIGVMYKIT
KTTDLRHFGGLIKGYPILGWTFFIAALSLAGIPPFSGFYGKFYIVRATFEKGFYLSGIIV
LLSSLIVLYSVIRIFLKGFFGEVEGYTLSKKVNVKYLTTIAVASTVITVIFGLSADTLFP
IIKDGAETFVDPSQYIHSVLGGK*

Sequence 2027
Contig_0696_pos_1081_776,
is similar to (with p-value 3.0e-40)
>gp:gp|AB015981|AB015981_6 Staphylococcus aureus genes for O
rfA, MnhA, MnhB, MnhC, MnhD, MnhE, MnhF and MnhG, complete c
ds. NID: g4001723.
atgcttatcattacatttttaactgagttaataaaagcaaactttggtgtactaaaaatt
attctcaaaccacgaattgagaataaacccggattctttgtgtacgagacggaattagaa
cgtgactggcaacttgttttactttccaacttgattacgttaacacctggcacagtcgtt
ttaggtattagtgatgaccgtaaaaagatttatatccactcaattgatttcagtacaaag
gaagaagagattcaaaatatcaaatcttcattagagaaggtcgttagaaaggtaggcgag
aaataa

Sequence 2028
MLIITFLTELIKANFGVLKIILKPRIENKPGFFVYETELERDWQLVLLSNLITLTPGTVV
LGISDDRKKIYIHSIDFSTKEEEIQNIKSSLEKVVRKVGEK*

Sequence 2029
Contig_0697_pos_2646_3434,
is similar to (with p-value 3.0e-34)
>sp:sp|P06696|TNPA_STAAU TRANSPOSASE A (TRANSPOSON TN554). >
pir:pir|A24584|A24584 transposition regulatory protein tnpA
- Staphylococcus aureus transposon Tn554 >gp:gp|X03216|ISTN5
54_1 Staphylococcus aureus transposon Tn554. NID: g43726. >g
p:gp|K02987|TRN554_1 Transposon Tn554 (from S.aureus), compl
ete, containing transposition genes tnpA, tnpB and tnpC, and
antibiotic resistance genes ermA and spc. NID: g154920.

gtgtatacttatactattaaaattagaaatgagattattatgaaaatagtagaagtaaaa
tctaagaatggtaccaattttatgattttagatggtaataatgaacctatagtagatgca
gtaagatatttgaagtatctggatagtgttaagaaaagtttaaataccaagaaaacctat
gcctatgcactaaaaaatttttttgtttacttagaaagtaaaaagatatgctataaagaa
gttagttttgataactttgttgattttataagatggatgaaaacacctttgaatatgag
aatgtcctctcttatcaccgaaaagaaaaaagcattagtcctaagacaattaatctgact
atgactgtagtatctaatttttatgattatctctataggagtaaaaaattagatgttaat
ttctatgattttatgcatatggaaagtaaatactctaaaaaatataaaagtttcatgcat
cacataaataaggactatagaacgttgaaaaatattttgaaagttaaagaaccaaagaaa
aaaatagaagtgttaactaatgcggaggttaagaaattattagaggaagctaataatatt
agagataaattcttaatacaattactatatgaaaccggattacgtataggtgaggtatta
tcattacgtattgatgatattaaatttgactttagaaacccatcgattaaaacgatacta
ggtggtacaggaatatcaacctgttatccatcgcctacgcctgtcggcctcagcttagga
cccgactaa

Sequence 2030
VYTYTIKIRNEIIMKIVEVKSKNGTNFMILDGNNEPIVDAVRYLKYLDSVKKSLNTKKTY
AYALKNFFVYLESKKICYKEVSFDNFVDFIRWMKTPFEYENVLSYHRKEKSISPKTINLT
MTVVSNFYDYLYRSKKLDVNFYDFMHMESKYSKKYKSFMHHINKDYRTLKNILKVKEPKK
KIEVLTNAEVKKLLEEANNIRDKFLIQLLYETGLRIGEVLSLRIDDIKFDFRNPSIKTIL
GGTGISTCYPSPTPVGLSLGPD*

Sequence 2031
Contig_0697_pos_5460_5116,
putative peptide of unknown function
gtgacaaaccggaggaaggtggggatgacgtcaaatcatcatgccccttatgatttgggc
tacacacgtgctacaatggacaatacaaagggcagcgaaactgcgaggtcaagcaaatcc
cataaagttgttctcagttcggattgtagtctgcaactcgactatatgaagctggaatcg
ctagtaatcgtagatcagcatgctacggtgaatacgttcccgggtcttgtacacaccgcc
cgtcacaccacgagagtttgtaacacccgaagccggtggagtaaccatttggagctagcc
gtcgaaggtgggacaaatgattggggtgaagtcgtaacaaggtag

Sequence 2032
VTNRRKVGMTSNHHAPYDLGYTRATMDNTKGSETARSSKSHKVVLSSDCSLQLDYMKLES
LVIVDQHATVNTFPGLVHTARHTTRVCNTRSRWSNHLELAVEGGTNDWGEVVTR*

Sequence 2033
Contig_0697_pos_1439_399,
putative peptide of unknown function
atgcaaaaagtacgttctgatataatgactcatcgtggttctcactatgatttaggagta
aagactgctctttggttacaaaccactcctttattaaaaaatcgaaataaagaatggcga
aagagaattccacgttttgatattgatgtcaaggaaacctatgatatatttcaaatctat
tcgccacagatttgggaagaaataattggtatgcaagatgtattgaatctacctacaaaa
caaatgattttaaattttggccattatcgatttactgatttaaaggacagtggttgcaca
gtatataaaggtcgtgatttttttagtccgaaattatgattatcatcctgcaacatatgat
ggtagatacttattatttcaacctaatgacgggggattatctcaaataggaccgacttca
agagtgactggtagaatggatggtatgaacgagtatggtttagttatggcatataatttt
atgcatcgtaaaaagcctgcaaatggatttgtatgttacatggttggtcggctaatactt
gaaaattgcaaaaatgtaactgaagcaatcaaatttttaaaggaagtaccgcatcgtagt
tcattcagttatatactaatggatagacattcgaattatgccattgtcgaagttacacct
cgatcaatagatgtaaggtatgaacatatatgcacaaatcattttgaattgcttacccat
gaaaatagaaactatacaagagaatctaaagaacgcttaaatcgtgtaataaataaaaca
actccttctacaaacaaagatatcgcattcaaattatttaacgacccgcaatacgaaatc
tatagcaacctatttaaaagttggtctggtacaattcatacttcactatatgaacctaat
tcattaatatcatggatggcattaggtcaaaacagtcatccaacctcaatcaatttttct
aattggttaaaaggaaagaaattgaatataaattactttgaaggcgaaatagatacacca
ttaacttttgccacatactaa

Sequence 2034

TGAAATATCTAATGAACACTATGTCAGACATAACACAAAAGTATTATCAAA
AATGATTTATGAACTTGCCTTAGAATTAACAAGTACAATTCGCTTTACTCC
TAGTGATAAAAAAGAAATAATTATAAGCGAATTCGTAGTTATGATATGATAG
CTTAAGTGTGTGTTTAGAATTAGAAAATAACTTTACACCTCATTGGCGATA
CTATAAATAAGAATAGAAAAAAGGGTTAGGAAGGGTGAGTGTTCAATGAGC
TTTGCATCAGATATGAAAAATGAACTAACACGCATAGAAGTTGACGAATCG
AATGCTAAAGCAGAGCTCAGTGCATTAATTCGCATGAATGGCGCACTTAGT
CTATCAAATCAACAGTTTGTAATTAATGTACAGACAGAAAATGCGACAACA
GCTCGTCGAATTTACTCTCTTATCAAACGTATATTTAATGTTGAAGTTGAA
ATTTTAGTTAGAAAAAAGATGAAATTGAAAAAAAACAATATTTATATATGT
CGAACAAAGATGTTAGCGAAAGAAATACTAAATGATTTAGGAATTTTAAAA
AAGGGAGTTTTTACTCACGATATTGATCCGGATATGATTAAAGATGATGAA
ATGAAAAGAAGTTATTTAAGAGGGGCTTTCTTAGCAGGTGGTTCTGTAAAT
AATCCTGAAACATCTTCATATCATCTTGAAATTTTTTCACAATATGAAGAT
CATTCCGAAGGTCTTACTAAATTGATGAATAGTTATGAACTCAATGCGAAA
CATTTGGAACGTAAAAAAGGGAGTATTGCGTATCTTAAAGAAGCTGAAAAA
ATTTCCGACTTTCTTAGTTTGATAGGTGGCTATCAAGCATTGTTAAAGTTT
GAAGATGTAAGAATTGTCCGTGATATGCGTAATTCGGTTAATCGTCTTGTT
AATTGTGAAACAGCAAATCTTAATAAAACTGTTAGCGCAGCAATGAAACAG
GTTGAAAGTATACAATTAATTGATGAAGAAATTGGGCTTGAAAATTTACCT
GATCGTTTAAGAGAAGTAGCGAAGCTCAGAGTAGAACATCAAGAAATATCG
TTAAAAGAATTGGGTGAGATGGTTTCTACAGGGCCTATATCTAAATCAGGT

Sequence 3821
step.1023e01.cons.ok
ATAAGTAATATTACACATAAATAAAATTGAATGCTATCACACTTATTAAGC
TTGTTATTAAAATATACATAAAGGAGGAGCGACGTGATAGGCAAACACTTT
ATTATAACTGGAGCAACGAGTGGGTTAGGTTTTGCAATAACCAATGAATTA
CTTCAAAGAGGGGCCCATGTTACTATACTTGCAAGAAATATAGATAAGTTC
AATCGAATCAAAGAAAACTATTTTAAACCTGAACATATCAATGTGATTAAA
TGTGATTTAATGCAACGAAAAGATATTGAATCATTACAAAAATTTTTAAAT
ACACCTATAAATGGTTTCATCTACAGTTCAGGTGTTGGATATTTTAAGTCT
ATAAGTGAGCATTCAACTCGTGAAGTAGTAGAAACTTACGAGGTTAATCTT
ACAAATTTTAATTTGTTATACAAAGTGATTCAACCACAATTAGTAAAAGCA
GCATATATCGTTGGTATATCTAGTCAAGCTGCTCTTGTTTCACAGGCTAAT
GCGGCACATTACGGTGCATCGAAAGCAGGGTTTAGCGCCGTTCTTAATGCA
TTGAGATTAGAACAACCGGAATTAAAAGTGCTCAATGTACAGCCCGGTCCA
ATAGATACACCATTCCAAAAAAACGCAGATCCTACTCTAAAGTATTTTAAA
AATTATAGACACATGATGATACAACCTCAACAACTTGCCAAGCAAATAGTG
GAAGGAATAATACTAAATAAAATTGAAATTAATCAACCATCATGGATGCAA
ATAATGCTTAAATTTTATCAATTATGTCCACGTACACTAGAAAAATTATGT
CCAAATCTATTTAAAAATAAAGTTTAAACACAGGTCAATTTTAAGGTAATC
AAAAGTATTGACTGAATGAACATTTTATAAATGATTTTTTCAAAAACTCAT
CTTTGGCTTTTGTCAACGTTATCAATATGATTTTTGTATTGCCTTAAAGTA
AAGAGATCCTACAGACGTCATTTAACCGTTTCATCTGTTGGATCTCTTTAT
TTAAGTATAGTCATCTAGGTATTTAACAAGTTGGTTAATATCCTTTTATTT
CAAATGTTGTGTATATTCAATATCTTTAACTCTATTACGTGCAGATTTGAT
TTGATCTAAACTGATTTCTTTATAATAATTGCGGACATTCTCTTCAAGTTG
TTCAACGCTACTAGCTCCTACAATAATTGACCCCATAGCATCATGAGAAGT
TAAATATTTAAATGATAACGCGGTTAAATTACTTTCCAATTCTTTAATAGA
AGCAATCGTGCTACCTAATTCGTCTTGAGTGTAATCTAACACACCGTTTTT
AAATTTTTCATCTATAACATCAACACTTTTTGAAGTTAATAAACCTTTAAA
TACAGGGCCACGTGCTAGAATTTTAACTTGCTTATCATGAACGTCATTAAT
AAGACTTTCAGGGCGATTATCTATTAAATTAAACTGGGACATAAGTGTTTC
AATTTGACTATTTTTAAGATAATAGTCTATCACGTTAGGCCGTATAGATGA
AATTCCATATGCACGAATATATCCTTCTTGCTTTAATTCATCAAATGCACT
AATAGTTTCGTCTAGAGGATCATCTATTGTTCCGCCATGTAATTGATATAA

GTCTAAATGGTTTAATCCTAATCGTTTCAATGATCCCTTAACACTTTCTTT
AATATGTTTTTTCGAAGGATCCCACGTCATATGTCCATCGTCAGTTAATCG
ATTTCCAACTTTAGTTCCGATAACGATGTCATCACGATTTTGATATTTTTT
TAAGGCTTTACCAACAATTTCTTCATTAACTCCTTGATCGTAAATATCTGC
AGTATCAAAATACGTAATACCATTATCAATTGCACTTTCAATAATTGGTTG
CGCTTTTTTATAATCTGTGCCTAAACTCATGCAACCTAACCCAAGTTCAGA
AATTTCGATGCCACTTTTTAGAATATTTTTTTGCATGTCCAGTCTCCTTTC
GATACACTTTAACTGACGAATTCAGTTTATCAATTTATAAAACCAATTAAA
AGGAACGTGTTTAAATATGAGATTAAACGAAAAAACAATCGATAGAACAGT
TATATATAATGGTAGTATTATTGATTTAGAAGTACATGATGTTGAATTACC
CGATGGTAGCACATCTAAACGTGAACTTGTATTTCATCATGGTGCGGTGGC
AGTGTGTGCAATAACTCCTGAAAATGAAGTTTTATTAGTTAAACAATTTCG
TAAGCCTGCAGATCAACCACTTTTGGAAATTCCCGCAGGCAAATTAGAAAA
GGGTGAAGATCGTAAAGAAGCGGCTATTAGAGAACTACAAGAAGAAACAGG
ATATATTGCTTCAGATTTGCAATTTGTCACTAATATGTATGGGTCTCCTGG
ATTTTCAAGTGAAAAACTTTCTATATACTTCACAGACCAATTAACGGTTGG
AGAAACCAATTTAGATGATGATGAATTTGTGGAGCTTCACAAAGTACCTTT
AAGTCAAATCGATTCATTGTTAAAAGATAATAAAATTGAGGATGCCAAAAC
AATCATTGCATTGCAACATCTATTATTAAATTATAATCATTCTAAATAACA
AGCAAATCTCCTTGCTTTTTACCGACAATATTGGTATTTTATTAAATGAAT
CATGGATTAAATTAAAATGATTATAATTCTTAGTAGAGGAGTGAGGCTTCC
GTGGAAGAACGATTAAATCGCGTGAAGCAACAATTACAACAATCTTCATAT
AAATTGACTCCACAAAGAGAGGCAACTGTTAGAGTATTAATTGAAAATGAA
AAAGATCATCTTAGCGCAGAAGATGTGTACTTAAAAGTCAAAGATAAGGCT
CCAGAAATAGGATTAGCTACCGTTTATAGAACTTTAGAATTGCTAGCTGAA
ATAAAAGTGCTAGATAAAATAAATTTTGGTGATGGTGTAGCTCGTTTTGAT
TTAAGAAAAGAAGGAGCCAAGCATTTCCATCATCA

Sequence 3822
step.1023e03.cons.ok
TGTACCACTTACTCCAAAAATATCTCCAAGAACGACATAACCTACGTAACC
GATTGTTGATAGAAGTAATATTCCCATTGCTTTTTTAAATTCTGGGTTATC
GGATTTGCCTTCGCTTTTGGCTTTAAGTGATGTTAAAGAAATACCTACAAC
CAATAAGATCATTGCTATAAGTCCCATCACTACTTGAACAATCGTGCTCCA
TTCACCTAAGAAAATAGCGCTAAATAGAGTGGTACCGACAAGTTGCATACC
CGTTGAAATAGGCATCGTTTTAGATACACCTATTAAATGCACTGATTTTAA
TTGATTACCTTGACCAAAAGCCCATAGAGCTCCTGATACTAAACCGACAAT
AATTACTGTAAGGTTATCAAACGCTGCGTGTCCAGTAGCAAGTAGAGAAAA
TCCGATAAAAAGTGTACCTAAAGTTGTACCTCGAATCTGATTATATGGTCC
ACCACCTACAAAAACATTTATAATGACTACACTACCCCAAAATAGGGCTGG
TAAAAGTGCTATCAAAAAATCTACAATTTGCACTTATTACTCACTCTCCTA
AGAACAAAATTAAGTGTCCCAATTACACTCGAAATCATTCTATAGTAATTA
AAAAAAGAAGTAAAAAACAACACCTTAAAAGTGTTGAAATTTTTAGTAAGT
AAATATTCGTATTAAGTGATAATGTGTTTTTGAACTATATGATTGAACAAG
ATATGTATATATAACTATCTTAATTAATTTTATATATAGTAATTTACAAAA
AGATACATGTTACAATGTATGTAATTCTATAACATGACGTATTTTATAAAT
GTGAAAGGAAAATTAAAATGAAATCTTTAATCTTAGCTGAAAAACCATCTG
TCGGAAGAGATATCGCTAATGCTTTGAATCTTCAACAAAAAAGTAATGGTT
ATATAGAAGGGAAACAGTATATAGTAACTTGGGCATTGGGGCATCTTGTGA
CAAATGCAACGCCTGAACAATATAACCCTTCATATAAAGAATGGAATTTAG
AAGACTTACCTATCATTCCTAAGAAAATGAAAACAGTAGTGATTAGTAAAA
CAAATAGACAATTTAAAATTGTAAAATCTTTAATTTTAGATAAAAATGTTA
AAGAAATTATTATAGCAACAGATGCTGGACGAGAAGGTGAACTAGTAGCTC
GTCTTATTTTAGATAAAGTAGGTAATAAAAAACCAATCAAGCGTTTGTGGA
TTAGTTCGGTTACAAAAAAAGCCATACAAGAAGGATTTAAACAGTTAAAAA
ATGGAAACGCGTATCAAAATTTATATGAAGCAGCACTTGCACGAAGTGAAG
CAGATTGGATAGTAGGGATTAATGCAACACGTGCACTAACGACAAAATATG
ATGCACAATTATCATTAGGTCGTGTACAAACTCCAACAATACAAATAGTTA

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
17 May 2001 (17.05.2001)

PCT

(10) International Publication Number
WO 01/34809 A3

(51) International Patent Classification[7]: C12N 15/31, C07K 14/31, 16/12, C12Q 1/68, G01N 33/53, A61K 39/085, 48/00

(21) International Application Number: PCT/US00/30782

(22) International Filing Date:
9 November 2000 (09.11.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/164,258 9 November 1999 (09.11.1999) US

(71) Applicant *(for all designated States except US)*: **GLAXO GROUP LIMITED** [GB/GB]; Glaxo Wellcome House, Berkeley Avenue, Greenford, Middlesex UB6 0NN (GB).

(72) Inventor; and

(75) Inventor/Applicant *(for US only)*: **KIMMERLY, William, John** [US/US]; 242 Via Villena, Encinitas, CA 92024 (US).

(74) Agents: **LEVY, David, J.**; Glaxo Wellcome Inc., Five Moore Drive, P.O. Box 13398, Research Triangle Park, NC 27709-3398 et al. (US).

(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*

(88) Date of publication of the international search report:
22 November 2001

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 01/34809 A3

(54) Title: STAPHYLOCOCCUS EPIDERMIDIS NUCLEIC ACIDS AND PROTEINS

(57) Abstract: S epidermidis polypeptides and DNA (RNA) encoding such polypeptides and a procedure for producing such polypeptides by recombinant techniques is disclosed. Also disclosed are methods for utilizing such polypeptides and DNA (RNA) for the treatment of infection, particularly infections arising from S epidermidis. Antagonists against the function of such polypeptides and their use as therapeutics to treat infection are also disclosed. Also disclosed are diagnostic assays for detecting diseases related to the presence of S epidermidis nucleic acid sequences and the polypeptides in a host. Also disclosed are diagnostic assays for detecting polynucleotides and polypeptides related to S epidermidis.

INTERNATIONAL SEARCH REPORT

International Application No
PC./US 00/30782

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12N15/31 C07K14/31 C07K16/12 C12Q1/68 G01N33/53
A61K39/085 A61K48/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07K C12N C12Q G01N A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
BIOSIS, MEDLINE, EMBL, EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE EMBL [Online] EBI; ACC.NO: M33228, 5 February 1991 (1991-02-05) BHAT ET AL.: "T.brucei kinetoplast ATPase 6 edited mRNA, complete cds." XP002163041 abstract --- -/--	1

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
16 March 2001	20. 06. 01

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	van Klompenburg, W

2

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Inter ional Application No
PC./US 00/30782

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	VAN DE KAMP ET AL.: "Elucidation of the primary structure of the lantibiotic epilancin K7 from Staphylococcus epidermidis K7. Cloning and characterisation of the epilancin-K7-encoding gene and NMR analysis of mature epilancin K7" EUROPEAN JOURNAL OF BIOCHEMISTRY, vol. 230, no. 2, 1 June 1995 (1995-06-01), pages 587-600, XP000990390 figures 3,4 ---	1-29
A	US 5 587 307 A (ALBORN JR WILLIAM E ET AL) 24 December 1996 (1996-12-24) column 2, line 28 - line 34; claims 1-5 ---	1-29
A	US 5 770 375 A (EDA SOJI ET AL) 23 June 1998 (1998-06-23) figure 2; tables 1-3 ---	1-29
A	US 5 961 975 A (KARAKAWA WALTER W ET AL) 5 October 1999 (1999-10-05) claims 1-12; examples 3-9 -----	19-29

2

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

national application No.
PCT/US 00/30782

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 21,26,27 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [X] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

see FURTHER INFORMATION sheet PCT/ISA/210

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [X] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-9, 11-29, all partially, 10 compl.

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: Invention 1; claims 1-9,11-29, all partially,
10 completely

An isolated polynucleotide comprising a member selected from the group consisting of: a) a polynucleotide encoding a polypeptide with at least a 70% identity to SEQ ID NO:2 b) A complementary polynucleotide. c) a polynucleotide comprising at least 15 sequential bases of the polynucleotide of (a) or (b).
A vector comprising said polynucleotide and a host cell comprising said vector. A process for producing a S. epidermidis polypeptide encoded by the above mentioned polynucleotide and a process for producing a cell which expresses said polypeptide. A polypeptide comprising an amino acid sequence which is at least 70% identical to SEQ ID NO:2. An antibody against a polypeptide comprising the amino acid sequence of SEQ ID NO:2. An antagonist which reduces or inhibits the activity of said polypeptide. A complex of said polypeptide and a binding molecule. A method of treatment, a method of diagnosis. A method to identify compounds capable of inhibiting the activity of said polypeptide. A method for inducing an immunological response. An immunological composition.

2. Claims: Inventions 2-1667; claims 1-9,11-29, all partially

As for invention 1, but each invention is limited to each one of the individual polypeptides with the sequences of the even numbers of SEQ ID NO: 4-3334 encoded by the polynucleotides with the sequences of the odd-numbers of SEQ ID NO:3-3334.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Present claims 20-22 relate to a compound defined by reference to a desirable characteristic or property, namely antagonising, inhibiting or reducing the activity of the polypeptide of the invention

The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compound by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the antibodies and antisense molecules with antagonist activity mentioned in the description at pages 32

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US 00/30782

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5587307 A	24-12-1996	AU 6180294 A	03-11-1994
		CA 2122202 A	31-10-1994
		EP 0625575 A	23-11-1994
		HU 70300 A	28-09-1995
		JP 6319561 A	22-11-1994
US 5770375 A	23-06-1998	AU 684250 B	11-12-1997
		AU 4513593 A	31-01-1994
		EP 0652291 A	10-05-1995
		JP 2965543 B	18-10-1999
		JP 10304895 A	17-11-1998
		JP 2965544 B	18-10-1999
		JP 10304896 A	17-11-1998
		JP 3026789 B	27-03-2000
		JP 10304897 A	17-11-1998
		WO 9401583 A	20-01-1994
		JP 2798499 B	17-09-1998
		KR 159071 B	16-11-1998
		US 5807673 A	15-09-1998
		US 5763188 A	09-06-1998
		US 5853998 A	29-12-1998
		US 5798211 A	25-08-1998
US 5961975 A	05-10-1999	US 5866140 A	02-02-1999
		AU 681573 B	04-09-1997
		AU 3074792 A	15-06-1993
		CA 2123811 A	27-05-1993
		EP 0648127 A	19-04-1995
		FI 942359 A	20-05-1994
		JP 7508498 T	21-09-1995
		NO 941877 A	16-06-1994
		WO 9309811 A	27-05-1993